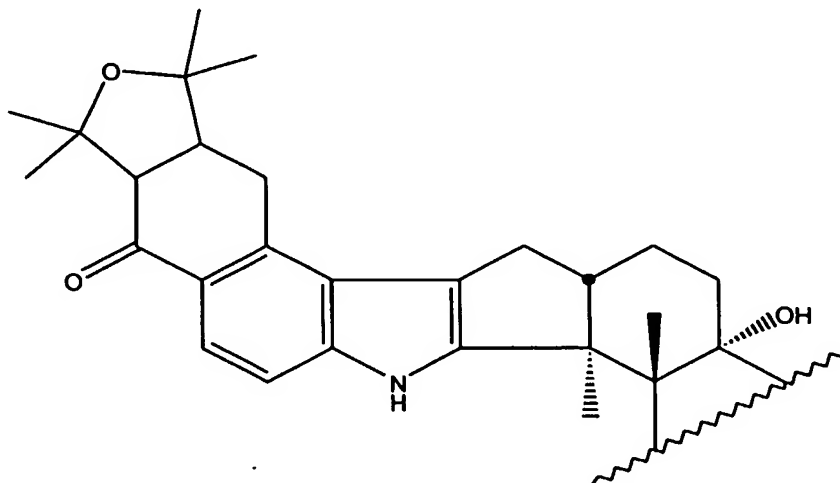


**WHAT WE CLAIM IS:**

1. A composition that contains a pharmacologically effective amount of at least one BK channel antagonist compound containing the moiety shown in structure (I):



STRUCTURE (I)

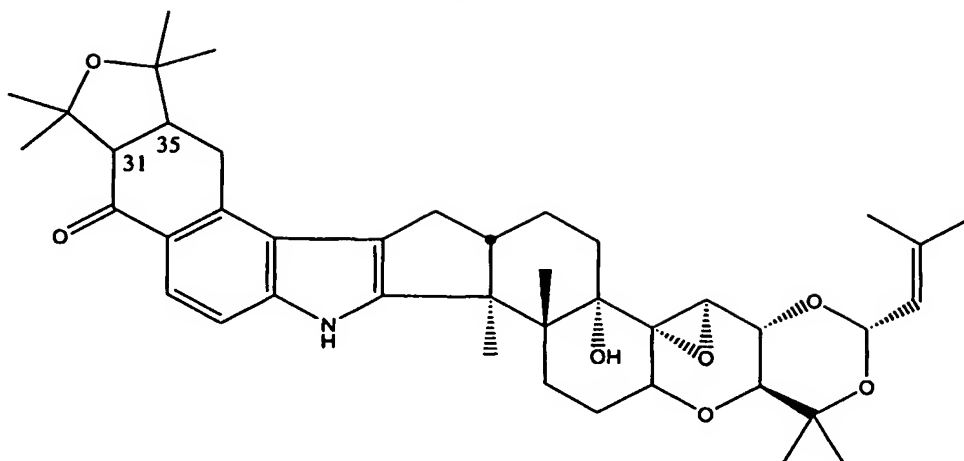
or derivatives thereof.

2. A composition as claimed in claim 1 wherein the derivatives of structure (I) are selected from the group consisting of: salts, analogues, isomers, and combinations thereof.

3. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is selected from the group consisting of: lolitrem B, lolitrem A, lolitrem F, 31-*epi*lolitrem F, 31-*epi*lolitrem B, lolitrem E, lolitrem E acetate, lolitrem L, lolitrem G, lolitrem C, lolitrem M, lolitriol, lolitriol acetate, lolitrem N, lolitrem J, lolitrem H, lolitrem K, lolicine A and B, 30-desoxy lolitrem B-30 $\alpha$ -ol, 30-desoxy-31-*epi*lolitrem B-30 $\alpha$ -ol, 30-desoxylolitrem B-30-ene lolilline and combinations thereof.

4. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (II):

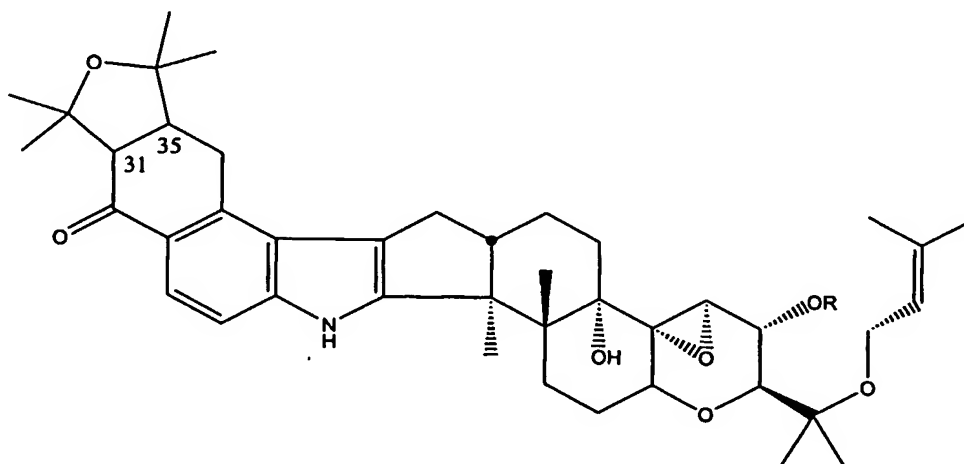
35



STRUCTURE (II)

which includes compounds selected from the group consisting of: lolitrem B = 31 $\alpha$ , 35 $\beta$  stereochemistry; 31-*epi*lolitrem B = 31 $\beta$ , 35 $\beta$  stereochemistry; lolitrem F = 31 $\alpha$ , 35 $\alpha$ ; 31-*epi*lolitrem F = 31 $\beta$ , 35 $\alpha$ .

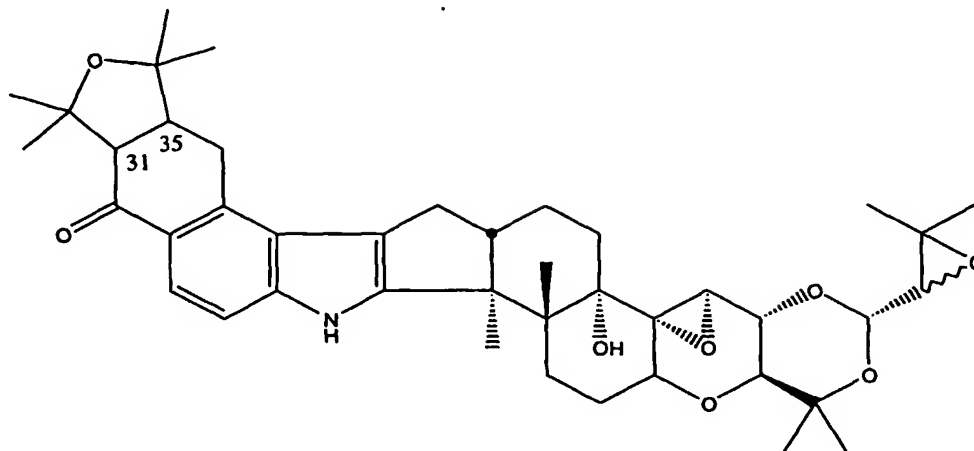
5. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (III):



STRUCTURE (III)

which includes compounds selected from the group consisting of: lolitrem E = 31 $\alpha$ , 35 $\beta$  stereochemistry where R = H or acetate; lolitrem L = 31 $\alpha$ , 35 $\alpha$  stereochemistry where R = H or acetate.

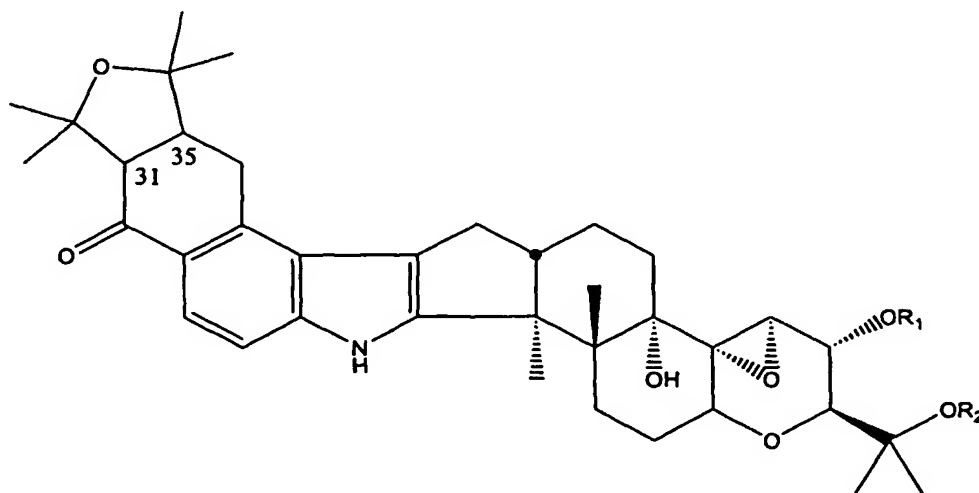
6. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (IV):



STRUCTURE (IV)

which includes compounds selected from the group consisting of: lolitrem A = 31 $\alpha$ , 35 $\beta$  stereochemistry; lolitrem G = 31 $\alpha$ , 35 $\alpha$  stereochemistry.

7. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (V):

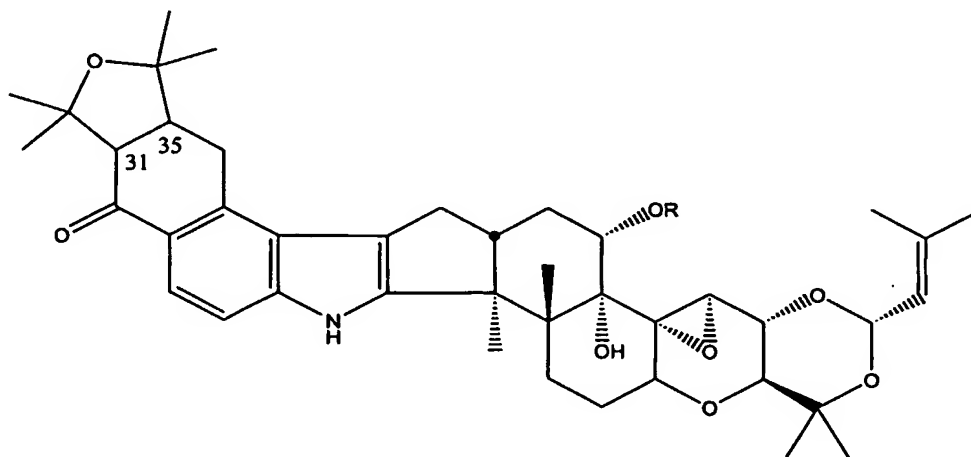


STRUCTURE (V)

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which includes compounds selected from the group consisting of: lolitriol; =  $31\alpha$ ,  $35\beta$  stereochemistry where  $R_1 = \text{H}$  or acetate and  $R_2 = \text{H}$ ; lolitrem N =  $31\alpha$ ,  $35\alpha$  stereochemistry where  $R_1 = \text{H}$  or acetate and  $R_2 = \text{H}$ ; Lolitrem J =  $31\alpha$ ,  $35\beta$  stereochemistry where  $R_1 = \text{H}$  or acetate and  $R_2 = \text{acetate}$ .

8. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VI):

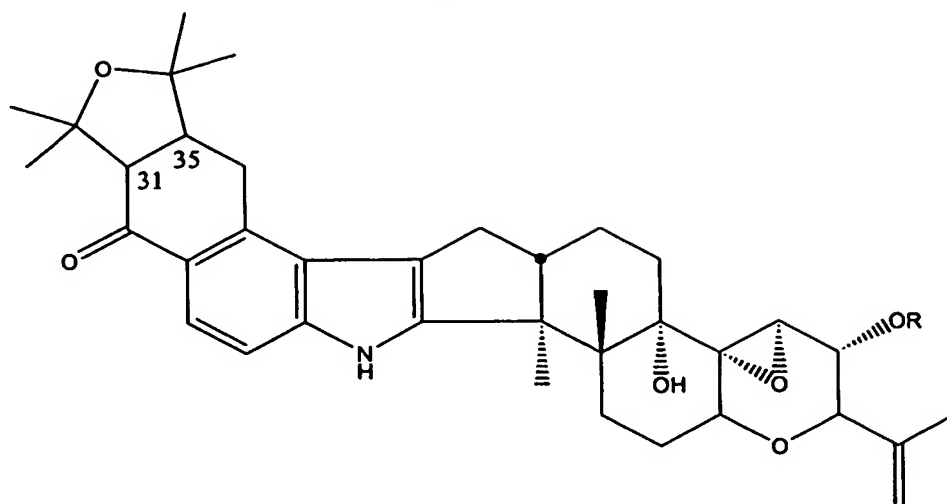


STRUCTURE (VI)

which includes lolitrem H =  $31\alpha$ ,  $35\beta$  stereochemistry where  $R = \text{H}$  or acetate.

9. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VII):

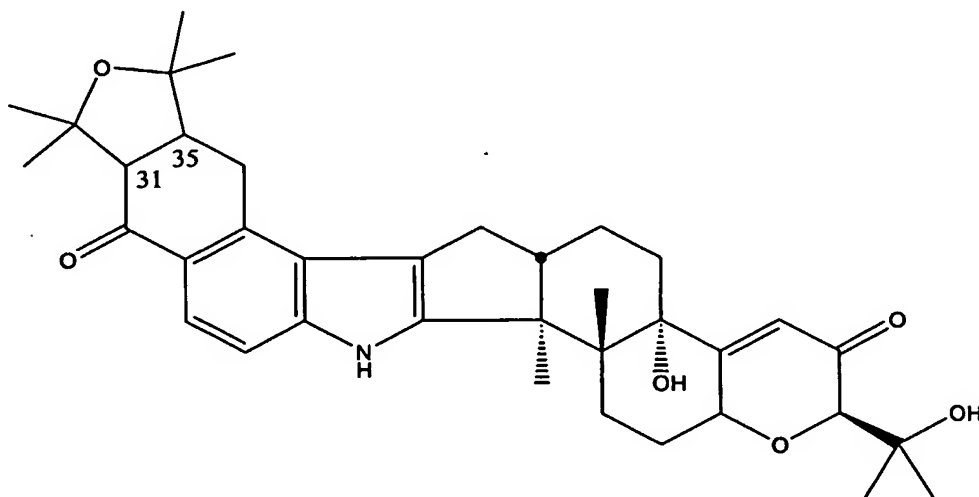
38



STRUCTURE (VII)

which includes lolitrem K = 31 $\alpha$ , 35 $\beta$  stereochemistry, where R = H or acetate.

10. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VIII):

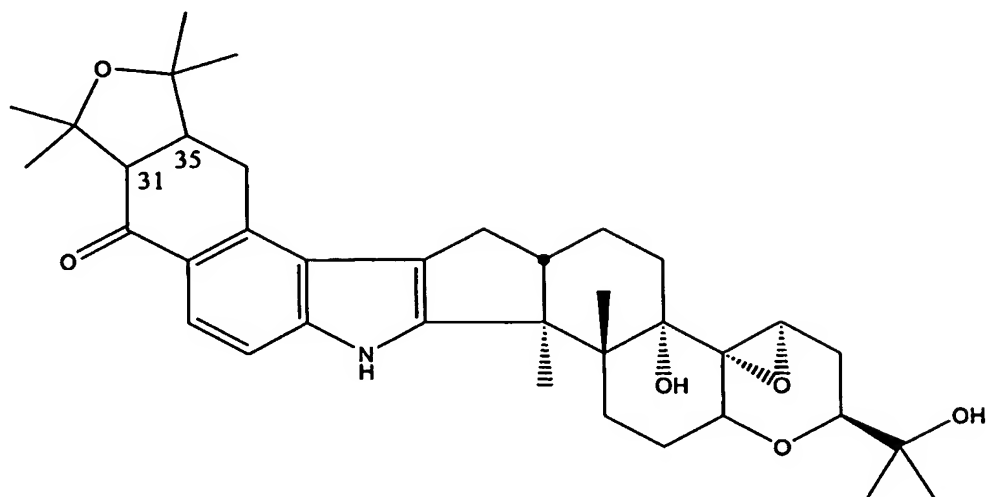


STRUCTURE (VIII)

which includes lolilline = 31 $\alpha$ , 35 $\beta$  stereochemistry.

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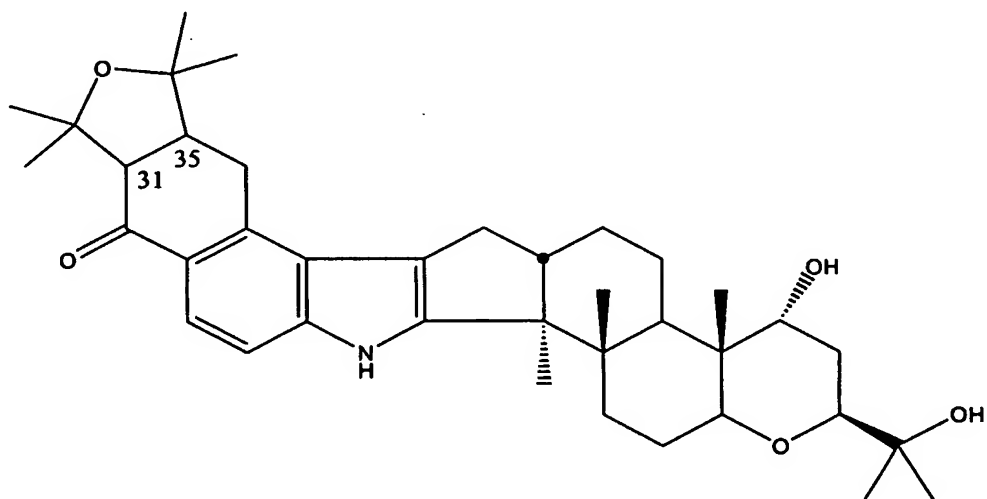
11. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (IX):



STRUCTURE (IX)

which includes lolitrem M = 31 $\alpha$ , 35 $\beta$  stereochemistry.

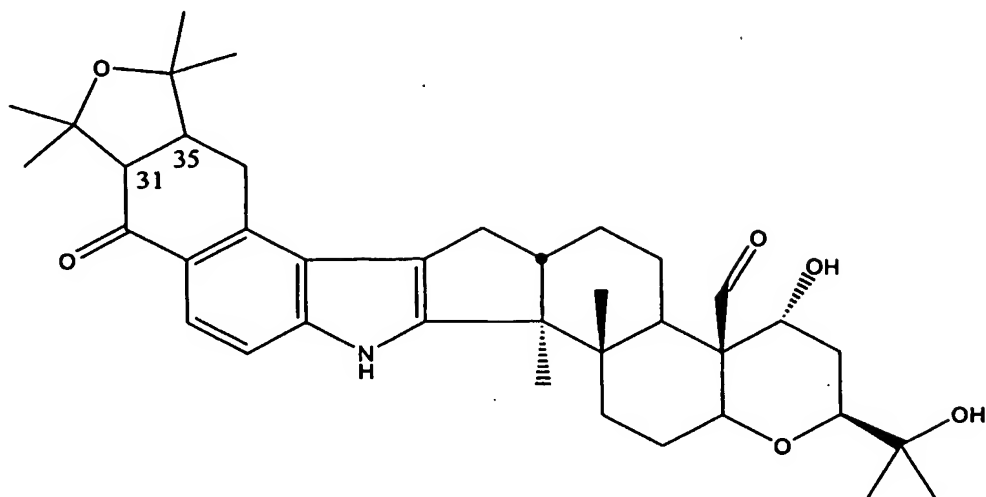
12. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (X):



STRUCTURE (X)

which includes lolicine A = 31 $\alpha$ , 35 $\beta$  stereochemistry.

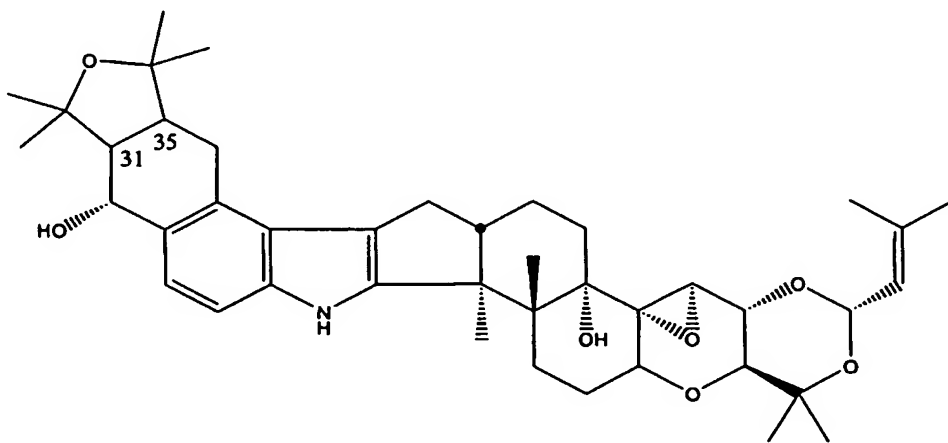
13. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (XI):



STRUCTURE (XI)

which includes lolicine B = 31 $\alpha$ , 35 $\beta$  stereochemistry.

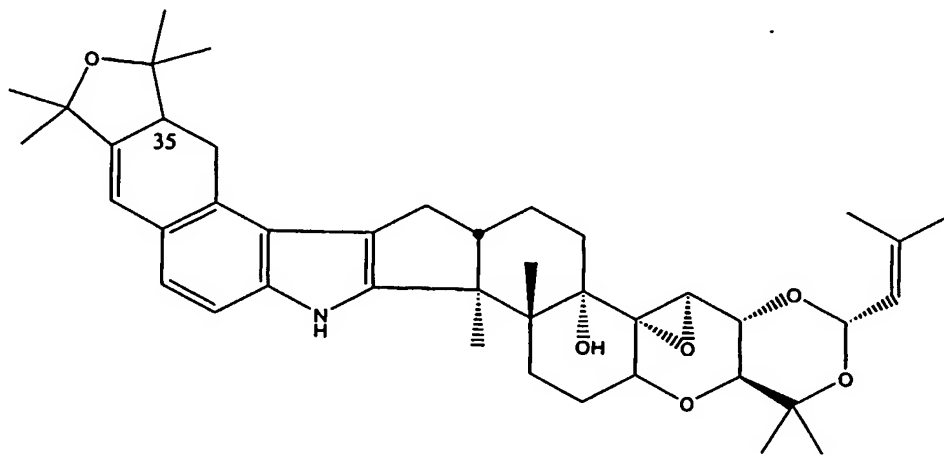
14. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (XII):



STRUCTURE (XII)

which includes compounds selected from the group consisting of: 30-desoxylolitre B-30 $\alpha$ -ol = 31 $\alpha$ , 35 $\beta$  stereochemistry; 30-desoxy-31-*ep*/lolitre B-30 $\alpha$ -ol = 31 $\beta$ , 35 $\beta$  stereochemistry.

15. A composition that contains a pharmacologically effective amount of at least one BK channel antagonist compound wherein the antagonist compound is structure (XIII):



STRUCTURE (XIII)

which includes 30-desoxylolitre B-30-ene = 35 $\beta$  stereochemistry.

16. A composition as claimed in any of the above claims wherein the composition further includes pharmaceutically and physiologically acceptable carriers.

17. A composition as claimed in claim 16 wherein the pharmaceutically and physiologically acceptable carriers include components selected from the group including; fillers; excipients; modifiers; humectants; stabilisers; emulsifiers; diluents; and other formulation components such as a use of a lipid vehicle.

18. A composition as claimed in any of the above claims wherein the composition is administered in a form selected from the group including: an injection; a tablet; a capsule; a suppository; an injection; a suspension; a drink or tonic; a syrup; a



powder; an ingredient in solid or liquid foods; a nasal spray; a sublingual wafer; a transdermal patch; a transdermal injection; and combinations thereof.

19. A composition as claimed in any of the above claims wherein the BK channel antagonist compound or compounds are extracted from endophyte-infected plants and seeds.

20. A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are extracted from fungal cultures.

21. A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are derived by chemical synthesis.

22. A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are extracted from heterologous expression systems including but not limited to bacteria, yeast, fungi, plants and animal cells.

23. A composition as claimed in claim 19 wherein the perennial ryegrass seed is from *Lolium perenne*.

24. A composition as claimed in any of the above claims wherein the BK channel antagonist compound or compounds has activity against both alpha ( $\alpha$ ) subunit and alpha plus beta ( $\beta$ ) accessory subunit ( $\beta_1$  to  $\beta_4$ ) channels.

25. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem B, the degree of antagonist inhibition is approximately 97% for a composition containing approximately 20nM lolitrem B.

26. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem B, the half maximal degree of antagonist inhibition ( $IC_{50}$ ) is found for a composition containing approximately  $3.7 \pm 0.4$  nM of lolitrem B.

27. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the

degree of antagonist inhibition is approximately 100% for a composition containing approximately 1000 nM lolitriol.

28. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the half maximal degree of antagonist inhibition ( $IC_{50}$ ) is found for a composition containing approximately 195 nM of lolitriol to inhibit  $\alpha$  and  $\beta_1$  BK channel activity

29. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the half maximal degree of antagonist inhibition ( $IC_{50}$ ) is found for a composition containing approximately  $536 \pm 16$  nM of lolitriol to inhibit  $\alpha$  and  $\beta_4$  activity.

30. A composition as claimed in any of claims 1 to 4 wherein, for 31-*ep*lolitrem B, the degree of antagonist inhibition is approximately 100% for a composition containing approximately 200nM 31-*ep*lolitrem B.

31. A composition as claimed in any of claims 1 to 4 wherein, for 31-*ep*lolitrem B, the half maximal degree of antagonist inhibition ( $IC_{50}$ ) is found for a composition containing approximately  $58 \pm 6$  nM of 31-*ep*lolitrem B to inhibit  $\alpha$  and  $\beta_1$  activity.

32. A composition as claimed in any of claims 1 to 4 wherein, for 31-*ep*lolitrem B, the half maximal degree of antagonist inhibition ( $IC_{50}$ ) is found for a composition containing approximately 49 nM of 31-*ep*lolitrem B to inhibit  $\alpha$  and  $\beta_4$  activity.

33. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem E, the degree of antagonist inhibition is approximately 100% for a composition containing approximately 100 nM lolitrem E.

34. A composition as claimed in any of claims 1 to 4 wherein the antagonist effect of the composition is not able to be reversed by wash out for concentrations of 10 nM or greater of lolitrem B compound.

35. A method of preventing repolarisation or hyperpolarisation of a cell, wherein the

cell contains a BK channel, including the administration to the cell of a pharmacologically effective amount of composition containing a BK channel antagonist as claimed in any of claims 1 to 34.

36. Use of a composition as claimed in any of claims 1 to 34 for preventing repolarisation or hyperpolarisation of a cell, wherein the cell contains a BK channel.